Prevalence of internal carotid artery stenosis in ambulatory patients presenting for non-emergent percutaneous coronary angiogram in a single Australian centre

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Abstract

Introduction: Association between coronary artery disease (CAD) and internal carotid artery stenosis (ICAS) could prove clinically relevant. However, evidence defining this association is currently inconclusive. Our study investigates the prevalence of ICAS in non-emergent, ambulatory patients presenting for PCA with suspected CAD in an Australian context.

Methods: Between February 2019 and June 2019, 121 consecutive participants were verbally consented and enrolled in our study. The data were analysed retrospectively. PCA and CUS were performed within 24 h of each other. Multinomial logistic regression assessed independent predictors for ICAS, with statistical significance set at P value < 0.05. Linear regression analysis correlated CAD and ICAS severity, with significance of a P-value < 0.05. Analysis was conducted using IBM SPSS 26 software (Chicago, Illinois).

Results: The final study included 121 patients (age 73 $\pm$ 9 years, 76.9% male). ICAS on CUS was present in 55.4% of participants for PCA. CAD was an independent risk factor for ICAS on multinomial logistic regression odds ratio 3.87 ($P = 0.023$). CAD severity (multi vessel disease) showed significant correlation with ICAS $r = 0.22$ ($P = 0.014$) using linear regression analysis.

Conclusion: CAD is an independent predictor of ICAS, and severity of ICAS is correlated with CAD disease. However, most participants had only minor ICAS (16–49% diameter stenosis). Our findings are consistent with internationally published studies, suggesting their data are generalisable to the Australian population. Larger studies are needed to address the applicability of CUS screening in patients with advanced CAD.

Keywords: coronary artery disease, carotid artery stenosis, Doppler ultrasound, percutaneous coronary angiogram, stroke.

Introduction

The Australian Institute of Health and Welfare identifies stroke as the leading cause of disability and third leading cause of death in individuals over the age of 75.[1]

The association between the degree of internal carotid artery stenosis (ICAS) and the risk of ischaemic stroke is well-documented.[2,3] There has been a decrease in the incidence of stroke in Australia over the last two decades. This is likely driven by primary and secondary prevention measures in combination with advances in acute management of strokes in hospital.[4-6] Despite these improvements in stroke management, the Australian government and stroke organisations are expecting an increase in the incidence of stroke. This is likely due to demographic shifts in particular, an ageing population.[5]

It is not known currently if an association between coronary artery disease (CAD) and ICAS is clinically significant and warrants preventative screening measures. Deploying a low-cost, non-invasive and accurate imaging modality to quantify ICAS severity in patients with suspected or known CAD may be beneficial in reducing catastrophic cerebrovascular events. Currently, carotid Doppler ultrasound (CUS) and percutaneous coronary angiogram (PCA) are standard

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imaging modalities for the monitoring of ICAS and CAD, respectively.

This study is the first in Australia to assess the prevalence of ICAS in ambulatory patients presenting for non-emergent PCA with suspected or known CAD. We additionally investigated whether monitoring ICAS yields clinically actionable information for managing patients with CAD. Lastly, we compared our results to internationally published findings and investigated any concordance.

Materials and methods

Study population

Between February 2019 and June 2019, consecutive participants presenting for non-emergent percutaneous coronary angiogram were verbally consented to an additional CUS within 24 h of the PCA at a single-centre metropolitan tertiary hospital. Inclusion criteria were all patients undergoing non-emergent PCA between February 2019 and June 2019. Exclusion criteria were any patients with cardiac electrophysiological pathology or past history of a heart valve replacement. The study participants resided in rural, outer metropolitan and metropolitan areas of Victoria, Australia. Participant variables recorded included present or prior tobacco use, diagnosis of diabetes mellitus, hypertension, dyslipidaemia or chronic kidney disease, or previous acute myocardial infarction, cerebrovascular events or coronary artery bypass grafting with participant medical information in Table S1.

Percutaneous coronary angiogram

Consecutive ambulatory patients underwent non-emergent conventional coronary angiography as previously described.[7,8] Coronary artery disease was based on cardiologist visual assessment, and a vessel with $\geq$ 30% stenosis was classified as a diseased vessel per international CAD reporting standards.[9]

Carotid Doppler Ultrasound

The carotid duplex ultrasound examination was performed using an Acuson S3000 Helix duplex ultrasound machine (Munich, Germany), with a 9–12 Multi-D linear transducer. Both right and left extracranial arteries were examined. Real-time B-mode images were recorded of the proximal, mid and distal regions of the common, internal and external carotid arteries. Per departmental protocol for carotid duplex ultrasound examination, the vertebral and subclavian arteries were investigated. Real-time imaging with peak systolic velocities and the Doppler waveforms were recorded in the subclavian arteries. Recording peak systolic velocities and flow direction assessed disease in the vertebral arteries. Colour Doppler was used to examine the arterial wall. Spectral Doppler traces were then recorded, measuring the peak systolic and end diastolic velocities to identify the presence of spectral broadening. The images were recorded on the hospital picture archival system, with each examination being reported by the consultant radiologist, using current 2008 ASUM criteria.[10]

Statistical analysis

IBM SPSS 26 (Chicago, IL) software was used for multivariate logistic regression analysis and linear regression analysis with post hoc analysis of variance where appropriate. Statistical significance was set at a P-value < 0.05.

Ethics approval

St. Vincent's Private Hospital Melbourne Ethics Review Board discussed the study design, concluding that due to the low risk and non-invasive nature of CUS, only verbal consent from the participant and treating cardiologist was required to enrol in the study. All study partcipants and treating cardiologists consented to enrolment in our study.

Results

The final study population included 121 participants, with the majority of our participants being of European origin and having a median age of 73 $\pm$ 9 years. The demographic information, medical history and indication for PCA are presented in Table 1. Major risk factors for CAD present in the study participants were hypertension and hypercholesterolaemia, each with 79.3%. 50.4% of participants were former or current smokers. This exposure rate is higher than the national age-matched average of 41.1%.[1] Diabetes mellitus was present in 25.6% of participants, which is slightly higher than the national age-matched average of 20%.[1] A majority (76.9%) of our study participants have CAD. This is likely because our participants are experiencing symptoms that are strongly associated with CAD, namely chest pain.[11] Chest pain was the most common indication for PCA in our study population at 64.5%. Shortness of breath was a secondary indication for PCA at 23.9%. Shortness of breath is also correlated with presence of CAD.[11] 29.8% of our study participants have a history of acute myocardial infarction; this is slightly higher than the national average, according to the Australian government, of 25.8%.[1] Again, this is likely because our study population has a propensity towards participants with a cardiac pathology. Very few participants in our study population had a history of a coronary artery bypass graft (CABG) (8.3%), or cerebrovascular event/ transient ischaemic attack (CVA/TIA) (6.6%). As this study was conducted in a private hospital, the prevalence of CABG or other cerebrovascular events amongst the population may not reflect the broader Australian population. A small minority of our patients had chronic kidney disease (CKD) (4.1%).

ICAS detectable by Doppler ultrasound was present in the majority of patients at 55.4%. Bilateral disease was present in 37.2% of the population, as highlighted in Table 2. A minority of patients showed disease of the subclavian (5%) and vertebral arteries (2.5%). A majority of patients with detectable ICAS presented with mild carotid stenosis (16–49%). These results

are consistent with other international reports.[12] A minority of participants (20.9%) presented with a 50–69% diameter reduction in the carotid artery diameter, representing moderate disease.[10] Two patients (3%) had 70–79% stenosis of the internal carotid artery, and two patients (3%) had 80-99% stenosis. There were no total ICA occlusions. These findings concur with contemporaneous reports,[12] although a report comparing CUS with CT coronary angiography by Cohen et al, found slightly higher rates of ≥70% ICAS in patients with CAD.[13]

In Table 3, multinomial logistic regression of cardiovascular co-morbidities and past medical history was performed to test for independent risk factors for ICAS. Only CAD was an independent predictor of ICAS in our study, odds ratio 3.87, P-value = 0.023. ICAS was defined as any stenosis ≥ 16–49% and CAD ≥ 1 coronary artery with ≥ 30% stenosis. Notably, cardiovascular disease risk factors such as age, sex, smoking status, as well as history of acute myocardial infarction, cerebrovascular event, coronary artery bypass graft, diabetes mellitus, hypertension, hypercholesterolaemia and chronic kidney disease were not independent predictors of ICAS in this study. These data provide evidence that there is a temporal association between CAD and ICAS as has been demonstrated in previous studies.[14]

Table 4 shows that the majority (76.9%) of participants in our study had detectable levels of CAD. This result is expected as clinical indications for PCA in our study population were strongly linked with CAD.[11] Given that CAD was an independent predictor of the presence of ICAS, we utilised linear regression analysis to determine the relationship between severity of ICAS and CAD. Regression modelling between the number of diseased coronary vessels and ICAS grade shows a statistically significant correlation between these two variables, with a P-value of < 0.014 and a correlational coefficient (R) of 0.22. These results are consistent with previous international large-scale reports.[12,13,15,16]

Table 1: Demographic and clinical characteristics of study population

Medical history	
Age, years	73 ± 9 years
Sex, male	93 (76.9%)
Diabetes mellitus	31 (25.6%)
Hypertension	96 (79.3%)
Hypercholesterolaemia	96 (79.3%)
Tobacco exposure	61 (50.4%)
Coronary artery disease	93 (76.9%)
Post-AMI	29 (29.8%)
Post-CVA/TIA	8 (6.6%)
Post-CABG	10 (8.3%)
CKD	5 (4.1%)
Indications for percutaneous coronary angiogram	
Chest pain	78 (64.5%)
Shortness of breath	29 (23.9%)
Medical Review	7 (5.8%)
Loss of consciousness	4 (3.3%)
Other	3 (2.5%)

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; CKD, chronic kidney disease; CVA, cerebrovascular event; TIA, transient ischaemic attack.

Discussion

These data indicate that the majority of patients who present for PCA in a non-emergent setting have ICAS. The majority of the ICAS are minor (16–49% diameter reduction) as defined by ASUM. Our results are consistent with other international reports.[12,13,16] Our data suggest that most participants in our study with ICAS are going to be managed conservatively. Conservative management of ICAS includes no medical therapy or medical therapy targeting critical risk factors associated with ischaemic stroke. Medical therapy currently addresses both lifestyle factors and pharmacological therapy.[17] Pharmacological therapy includes agents which target cardiovascular risk factors that are associated with an increased arterial plaque burden, including targeting of hypertension,[18] decreasing low-density lipoprotein levels via statins,[19,20] utilising low-dose aspirin for its antiplatelet properties[21] and management of diabetes mellitus.[22] Medical therapy used to treat ICAS for the primary and secondary prevention of stroke is identical to the lifestyle and

Table 2: Internal carotid artery stenosis prevalence and severity

Prevalence	
Carotid artery stenosis	67 (55.4%)
Bilateral carotid stenosis	45 (37.2%)
Subclavian artery stenosis	6 (5.0%)
Vertebral artery stenosis	3 (2.5%)
Severity of Internal Carotid Artery Stenosis per ASUM Criteria (% of ICAS)	
16–49% diameter reduction	49 (73.1%)
50–69% diameter reduction	14 (20.9%)
70–79% diameter reduction	2 (3.0%)
80–99% diameter reduction	2 (3.0%)

Table 3: Multinomial logistic regression of cardiovascular risk factors and carotid artery stenosis

CVD risk factors	Odds Ratio (95% Confidence Interval)	P-value
Age, >75 years old	2.06 (0.85–4.97)	0.11
Sex, male	0.56 (0.18–1.76)	0.32
Diabetes Mellitus	1.28 (0.48–3.40)	0.63
Hypertension	2.42 (0.76–7.68)	0.13
Hypercholesterolaemia	0.36 (0.11–1.32)	0.10
Tobacco exposure	2.78 (0.97–5.38)	0.06
Coronary artery disease	3.87(1.20–12.42)	0.02
Post-AMI	1.38 (0.51–3.74)	0.50
Post-CVA/TIA	2.40 (0.36–16.06)	0.38
Post-CABG	3.51(0.39–31.36)	0.26
CKD	1.39 (0.019–10.09)	0.74

Abbreviations same as Table 1.

Table 4: Prevalence of diseased coronary arteries and linear regression analysis between ICAS and CAD

Prevalence	
NAD	28 (23.1%)
1 vessel disease	37 (30.6%)
2 vessel disease	29 (24.0%)
3 vessel disease	25 (20.7%)
4 vessel disease	2 (1.7%)
Linear regression analysis	
$R = 0.22$	P-value = 0.014

medication regimen used to treat CAD. Therefore in our study when patients are being optimally treated for CAD, they are also likely being treated optimally for ICAS.

The only independent predictor of ICAS, in our study, was the presence of CAD. This result is likely due to the inclusion criteria of cardiac symptoms selecting for a cohort likely to have pre-existing CAD. As other studies have shown that the demographic, co-morbid conditions and past medical history data collected in Table 1 contribute to the development of ICAS.[23-25]

Finally, there was a statistically significant correlation between the number of diseased coronary vessels and the degree of ICAS. Critically, these results suggest that there is an association between ICAS and significant CAD. Therefore, there is a role for CUS screening in patients with known, or a high likelihood of advanced CAD.

Conclusions

Our study is the first Australian report to investigate the prevalence of ICAS in a non-emergent, ambulatory population in a single Australian tertiary centre. We found that ICAS is present in the majority of patients presenting for PCA with suspected or known CAD. Furthermore, we find that the presence of CAD is an independent predictor of the presence of ICAS. Moreover, there is a discrete relationship between the number of diseased coronary arteries and the degree of ICAS. We also note the majority of patients in our study had only minor ICAS. This study was limited by its private hospital setting, with some co-morbid conditions and advanced diseased states more likely to be managed in public hospital settings. Additionally, the majority of patients in the study were male of European descent. Therefore, to enhance the generalisability of these results, a more diverse cohort should be examined in future studies. While we acknowledge the limitations of our study, we also conclude that our results are in concurrence with other large-scale international reports, suggesting that those studies can likely be generalised to the Australian population. Future longitudinal studies addressing the role of key cardiovascular risk factors may provide more specific data, beyond logistic regression analysis, about interactions between CAD and ICAS especially those risk factors that approach statistical significance. Further, future studies that include parameters like carotid intimal–medial thickness and vascular plaque morphology may contribute additional vectors of clinically relevant information for stratification of cardiovascular and cerebrovascular risk, as

much research has been done in these areas. However, incorporation of these parameters has yet to be translated into routine clinical practice on CUS examinations. Finally, examining advanced CAD states and the concomitant severity of ICAS to further extrapolate a relationship are warranted as has been suggested by our results.

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Conflict of interest

The authors declare no conflict of interest.

Authorship statement

All authors agree the submission is original research and has been written by the authors as stated. Additionally, the work has not been published elsewhere.

Author contribution

Andrew James O'Brien: Conceptualization (lead); Data curation (equal); Formal analysis (lead); Methodology (supporting); Project administration (lead); Writing-original draft (lead); Writing-review & editing (lead). **John Donlan:** Conceptualization (supporting); Data curation (equal); Formal analysis (supporting); Project administration (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **John I Vrazas:** Conceptualization (lead); Data curation (supporting); Formal analysis (lead); Project administration (lead); Supervision (lead); Writing-original draft (lead); Writing-review & editing (lead).

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1 Medical history and CUS results.

